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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,856	06/21/2001	Martha Jo Whitehouse	PP16090.004 (35784/235886	6233

7590 12/23/2002

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/23/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,856	WHITEHOUSE, MARTHA JO	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-82* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Election/Restrictions

1. Applicant's election with traverse of FGF-2 (SEQ ID NO: 4) in Paper No. 9 (28 October 2002) is acknowledged. The traversal is on the ground(s) that SEQ ID NO: 2 and SEQ ID NO: 4 are structurally similar molecules only differing by two amino acid residues (positions 112 and 128) and perform similar functions. This is found persuasive. Applicant's election without traverse of heparin in Paper No. 9 (28 October 2002) is acknowledged. Claims 1-82 will be examined to the extent that they read on FGF-2 (SEQ ID NO: 2, 4, 6, and 8).

Status of Application, Amendments, and/or Claims

2. Claims 1-82 are under examination.

3. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Priority

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application (60/213504) upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-82 of this application. The provisional application (60/213504) does not disclose SEQ ID NO: 4 or heparin, nor the therapeutic uses of either.Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. Provisional applications 60/276549 and 60/264572 are both provide adequate support under 35

U.S.C. 112 for claims 1-82. Therefore, the claim for domestic priority is granted to provisional application 60/264572 with a filing date of 26 January 2001.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pp. 18 line 3). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

7. Claims 1-82 are objected to because of the following informalities: the claims read on non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 refers to Figures 2, 3, 4, and 5 thus the claim is incomplete.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 6440934 in view of Moyer et al. (1998). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of US 6440934 describes a method comprising administering a therapeutically effective amount of a recombinant fibroblast growth factor-2 (FGF-2) or an angiogenically active fragment or an angiogenically active mutein thereof into one or more coronary vessels or into a peripheral vein of a human patient said therapeutically effective amount being about 0.2 μg/kg to 48 μg/kg of patient weight thus meeting the limitations of claims 1-82 of the instant Application 09/886856.

10. Regarding coronary artery disease reading on peripheral artery disease in the instant application (09/886856), the art recognizes the utility of using bFGF also known as FGF-2 for treatment of peripheral artery disease such as ischemia or claudication (pp. 1434 "bFGF in experimental vascular insufficiency: peripheral vascular disease and ischemic heart disease") thus meeting the limitations of claims 1-73 (Moyer et al., 1998).

11. Regarding administration of FGF-2 as bFGF or SEQ ID NO: 2, the art recognizes that FGF-2 is also known as basic fibroblast growth factor (pp. 1426 second paragraph) and a sequence search of the Issued Patents database shows that SEQ ID NO: 2 of this instant

application (09/886856) is identical to the SEQ ID NO: 2 of US 6440934 thus meeting the limitations of claims 1-82 (Moyer et al., 1998; SEQ Search Results of Issued Patents Database).

12. Regarding administration of FGF-2 via intra-arterial infusion (IA), intramuscular injection (IM), intravenous infusion (IV), and subcutaneous injection (SC) the art recognizes that these are means of administering a therapeutic agent to a patient. US 6440934 claims the administration of FGF-2 to a peripheral vein, intravenous, intracoronary administration, and infusion. A person of ordinary skill in the art at the time of the invention would have known to make any necessary modifications to improve administration based US 6440934 thus meeting the limitations of claims 2, 6, 40-42, and 63-64 (US 6440934 Col. 29 claim 1; Col. 31 claim 6, 8, 14, 16, 17; Col. 32 claim 21-22, 24, 26, 28, 30, 32-34, 35; Col. 33 claim 48-49; Col. 34 claims 54, 57).

13. Regarding administration of FGF-2 via common femoral artery the art recognizes that administration into a femoral artery as an applicable route of administration for FGF-2 in treating intermittent claudication thus meeting the limitations of claims 1-82 (Moyer et al., 1998 pp. 1435 "5.2 bFGF in rats with experimental intermittent claudication").

14. Regarding claudication, critical limb ischemia the art recognizes the use of bFGF in the treatment of experimental intermittent claudication and chronic critical leg ischemia via administration of bFGF to femoral arteries thus meeting the limitations of claims 7, 8, 65-73 (Moyer et al., 1998 pp. 1435-1436 "5.2 bFGF in rats with experimental intermittent claudication" and "5.3 bFGF in rats with experimental chronic critical leg ischemia").

15. Regarding heparin co-administration the US 6440934 claims the co-administration of heparin with FGF-2 (including recombinant FGF-2) in a pharmaceutical composition thus

meeting the limitations of claims 49-50 (US 6440934 Col. 30 claims 2-3, Col. 31 claims 16, 18; Col. 32 claims 22, 37; Moyer et al., 1998 pp. 1426 second paragraph).

16. Regarding dosages, dosage regiments, and FGF-2 administration as an adjuvant to vascular surgery, mechanical bypass surgery, angioplasty, and angiogram, the art recognizes that bFGF has pleiotropic beneficial effects of angiogenesis and increasing wound healing. Moyer et al. (1998) also notes that bFGF treatment has been performed on patients undergoing elective coronary artery bypass thus meeting the limitations of claim 23 (Moyer et al., 1998 pp. 1437 first paragraph and "5.5 bFGF and vascular protection and healing").

17. Regarding improvement in peak walking time (PWT), reduction in body pain, improvement in stair climbing ability, reducing the severity of claudication, the art recognizes these as clinical endpoints or measures of the clinical effectiveness of a therapy thus meeting the limitations of claims 43-47 (US 6440934 Col. 33 claim 45; Col. 34 claims 51-52).

18. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use bFGF (FGF-2) to treat peripheral artery disease because of its low toxicity and utility in providing relief in ischemia, claudication, and neurodegenerative models (Moyer et al., 1998 pp. 1429-1434 "3. Neuroprotective efficacy of bFGF in *in vitro* models of cell death and ischemia" and "4. Neuroprotective and recovery enhancing effects of bFGF in animal models").

19. The person of ordinary skill in the art at the time of the invention would have been motivated to make those modifications because bFGF at the time of the invention was seen as a promising therapeutic molecule by which coronary artery disease and injury including peripheral artery disease could be prevented and treated. In addition, bFGF was seen a valuable molecule to

speed or improve healing from cardiovascular surgery or treatment (Moyer et al., 1998; pp. 1437 first paragraph and pp. 1437-1439 "bFGF and vascular protection and healing" and "6.Conclusions").

20. The person of ordinary skill in the art at the time of the invention would have a reasonable expectation of success because of success in using bFGF in animal models and clinical use in coronary bypass surgery (Moyer et al., 1998; pp. 1437).

Summary

21. Claims 1-82 are hereby rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, Ph.D. whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D. can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
December 18th, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER